

TOBACCO INDUSTRY RESEARCH COMMITTEE  
150 EAST FORTY SECOND STREET NEW YORK 17, N. Y.

Application For Research Grant

#213  
(Cf. #3381 - Activated  
2/1/55  
Renewed - 2/1/56  
and #160 - Activated 8/1/57  
8/1/57

Date: September 10, 1958

1. Name of Investigator:
  - a) Marion B. Sulzberger, M.D.
  - b) Walter Hedisch, M.D.
  - c) Kurt DeCrisis, M.D.
  - d) Vincent Fontana, M.D.
2. Title:
  - a) Professor and Chairman, Dept. of Dermatology & Syphilology, New York Univ. Bellevue Med. Center, Post-Graduate Medical School
3. Institution:
  - b) Associate Professor Clinical Medicine, NYU College of Medicine.
  - c) Clinical Assistant
- & Address:

New York University - Bellevue Medical Center  
550 First Avenue, New York 16, New York
4. Project or Subject:

Investigation of the effects of tobacco on the human vascular system, based on the fact that certain tobacco effects are due to allergic susceptibility of specific individuals rather than to obligatorily toxic products in tobacco smoke. And that patients with occlusive vascular diseases respond differently than healthy smokers.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

In the past two years our studies have shown that in about 30% of healthy subjects plethysmographically measured blood flow to the lower extremities decreased significantly (2 ml./100 cc/min. or more) for a transient period of time. 90% of these subjects who were negative on skin testing with tobacco extracts had no change in blood flow.

Thirty patients with clinically documented non-gangrenous obliterative arteriosclerosis of the lower extremities have been tested so far. Thirteen of these had a significant (2 ml./100cc./min. or more) increase in plethysmographically measured blood flow to the lower extremities in response to tobacco smoking. The remaining 17 patients showed no change; none had a significant decrease.

These most puzzling findings urgently call for an extension of the study:

- 1) Further confirmation by increasing the number of test subjects in this group.
- 2) Testing of at least three more groups with other types of occlusive arterial disease, namely, patients with TAO\* patients with occlusive disease of small blood vessels and patients with "arteriospastic" disorders (Raynaud's reflex dystrophy) Vascular responses tested as before in association with intradermal testing with tobacco extracts.

\* TAO - Thrombo-angitis Obliterans

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While no explanation can be offered at present for the surprising fact that some patients with OAS\*\* responded to tobacco smoking with vasodilation, it appears likely that this bears some relationship to altered vasomotor responses. Alterations of vasomotor responses in patients with various neurologic lesions have been under investigation by our group for the past several years. Studies of the basic mechanisms responsible for the constriction and dilation of blood vessels in man are in progress.

It is planned to carry out the following experiments to establish whether or not specific allergic sensitization plays a basic role in vascular reactions to tobacco smoking.

(A) Patients with various vascular and other diseases which have sometimes been regarded as being made worse by smoking will be skin-tested to ascertain whether their skin reactions are in higher incidence or greater intensity than those of control subjects of equivalent age and exposure to tobacco.

(B) Vascular responses are to be tested by automatic recording of surface temperature and venous occlusion large limb plethysmography in a constant temperature humidity room, under environmental conditions set at 20°C temperature with 55% humidity.

Four groups will be studied:

1. Healthy volunteers - smokers.
2. Healthy volunteers - non-smokers.
3. Patients with occlusive vascular disease - smokers
4. Patients with occlusive vascular disease - non-smokers.

ECG before and after smoking will be done on all patients.

(C) The results will be correlated with the results of skin-testing and clinical symptomatology.

(D) All the skin test reactions from the battery of tobacco extracts will be statistically analyzed, not only in regard to host factors (such as age, tobacco exposure, smoking, allergic and hereditary constitution, disease, etc.), but also in regard to relative capacity of various brands and types of tobacco to produce sensitization of the vascular tree ("index of sensitization", "relative sensitization potential").

\*\* OAS - Obliterative Arterio-Sclerosis

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6. Budget Plan:

Salaries	10,000	per annum
Expendable Supplies	500	" "
Permanent Equipment	2,000	" "
Overhead	2,000	" "
Other	500	" "
Total	15,000	

7. Anticipated Duration of Work: **Two years**

8. Facilities and Staff Available:

**Complete facilities and patients and selected staff of the Departments specified above at the New York Skin and Cancer Unit, University Hospital, Bellevue Hospital, Gouverneur Hospital and other teaching services of New York University-Bellevue Medical Center.**

9. Additional Requirements:

**Supply of pure tobacco of different types and origin, cigarette tobacco of different brands.**

10. Additional Information (Including relation of work to other projects and other sources of supply):

**All workers concerned are intimately familiar with the essential problems, having been engaged in this study for at least 2 years.**

Signature /s/ Marion E. Sulsberger  
Director of Project

/s/ Edward F. Smith  
Business Officer of the Institution

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